SCIENTIFIC ABSTRACT

The overexpression of the HER-2/*neu* oncogene in 30% of ovarian and breast cancers is associated with enhanced metastatic potential, drug resistance and poor survival. The E1A gene obtained by deleting the transforming element (E1B) from the E1 region gene of the human adenovirus type 5, functions as a tumor suppressor gene when transfected in cancer cells which overexpress the HER-2/*neu* oncogene. E1A expression induces downregulation of the HER-2/*neu* p185 oncoprotein by transcriptional control. This downregulation results in the loss of the malignant phenotype in tissue culture and in animal models. It also results in long-term, tumor-free survival of SKOV-3 human ovarian cancer bearing *nu/nu* mice treated with E1A Lipid Complex (E1A plasmid complexed to the cationic lipid gene delivery system comprised of DC-Cholesterol* and DOPE**). We propose to treat 12-24 patients with metastatic or unresectable solid tumors overexpressing HER-2/*neu* with the E1A Lipid Complex administered by the intratumoral route at 4 dose levels according to a repeated dose schedule of 3 daily doses followed by weekly doses through Day 50. These treatment courses will be repeated until disease progression or excessive toxicity is observed. The objectives of the trial will be to determine whether E1A transfection and HER-2/*neu* downregulation can be documented in cancer cells biopsied from the tumor, to determine the maximum biologically active dose or the dose limiting toxicity, to evaluate the overall safety profile, and to detect any antitumor activity and its correlation to HER-2/*neu* downregulation.